

PATENT ABSTRACTS OF JAPAN

(11)Publication number : **2000-266753**

(43)Date of publication of application : **29.09.2000**

(51)Int.CI. **G01N 33/68**

G01N 31/00

(21)Application number : **11-076011** (71)Applicant : **FUJI PHOTO FILM CO LTD**

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(54) MEASURING METHOD FOR THIOL-GROUP-CONTAINING COMPOUND

(57)Abstract:

PROBLEM TO BE SOLVED: To provide a method conveniently and accurately measuring a thiol- group-containing compound such as alkylthiol included in a sample such as a tissue section.

SOLUTION: This measuring method for a thiol-group-containing compound includes the following processes. (1) A process contacting a liquid, a solid, or a gas sample comprising a thiol-group-containing compound to a dispersion liquid comprising metal particulate such as silver (for example, colloidal silver). (2) A process detecting a change of state such as a color change of the dispersion liquid and/or a coagulation of the metal particulate occurring due to an interaction between the thiol-group-containing compound and the metal particulate. The average particulate size of the metal particulate is preferably 0.001 µm to 0.5 µm. In addition, a substance selected from a group comprising alkylthiols, arylthiols, amino acid and it's derivative, and protein is preferable as the thiol-group containing compound.

[Claim(s)]

[Claim 1] It is the measuring method of a thiol group content compound, and is following production process: (1). Production process; and (2) to which a solution which contains a thiol group content compound in dispersion liquid containing a metal particle, a solid-state, or a gaseous sample is contacted A method including a production process which detects a change of state of the above-mentioned dispersion liquid produced by interaction of a thiol group content compound and a metal particle.

[Claim 2] a metal particle -- a grounder -- id -- a method according to claim 1 of being a condition.

[Claim 3] A method containing a metal chosen from a group which consists of the 8th group of an element periodic table, the 9th group, the 10th group, the 11th group, and the

12th group according to claim 1 or 2.

[Claim 4] A method given in claim 1 containing a metal chosen from a group which a metal particle becomes from the 4th period of an element periodic table, the 5th period, and the 6th period thru/or any 1 term of 3.

[Claim 5] A method containing a metal chosen from a group which a metal particle becomes from gold, silver, copper, and platinum according to claim 1 or 2.

[Claim 6] mean particle diameter of a metal particle -- 0.001 mum -0.5 mum it is -- a method given in claim 1 thru/or any 1 term of 5.

[Claim 7] A method given in claim 1 which detects change of a color of dispersion liquid, and/or condensation of a metal particle as a change of state of dispersion liquid thru/or any 1 term of 6.

[Claim 8] A method given in claim 1 which is the material chosen from a group which this thiol group content compound becomes from alkyl thiols, aryl thiols, amino acid, its derivative, and protein thru/or any 1 term of 7.

[Claim 9] A reagent which is a reagent for measurement of a thiol group content compound, and contains dispersion liquid containing a metal particle.

[Claim 10] A reagent according to claim 9 which produces a change of state by interaction with a thiol group content compound.

[Claim 11] Dispersion liquid which contain a metal particle for using it for a method of a publication in claim 1 thru/or any 1 term of 8.

DETAILED DESCRIPTION

[Description of the Prior Art] it reacts to detection and the quantum of a thiol group content compound with the method of measuring directly using separation analysis means, such as a gas chromatography and liquid chromatography, and thiols, such as a maleimide derivative, and the compound which reacts -- making -- detection of a fluorochrome etc. -- the method of detecting, after combining an easy compound is learned. However, the problem of necessity in skill is in large-scale equipment or actuation at these methods.

[0003]

[Problem(s) to be Solved by the Invention] The technical problem of this invention is to offer the method of measuring a thiol group content compound simple and correctly. It is more specifically offering the method of measuring simple and correctly thiol group content compounds, such as alkyl thiols, aryl thiols, a cysteine, a glutathione, and protein. Moreover, another technical problem of this invention is to offer the reagent used for measurement of the above-mentioned thiol group content compound.

[0004]

[Means for Solving the Problem] If this invention persons contact a sample of a liquid which contains a thiol group content compound in dispersion liquid which distributed a particle containing metals, such as silver, as a result of inquiring that the above-mentioned technical problem should be solved, a solid-state, or a gaseous state An interaction arises between thiol group content compounds and metal particles which are contained in a sample, and condensation of a change metallurgy group particle of a color tone arises in dispersion liquid, It found out that a thiol group content compound in a sample could be measured simple and correctly by detecting change of this color tone, and change of a state of aggregation of a particle with viewing, an optical microscope, or

a spectroscopy-means in a list. This invention is completed based on these knowledge. [0005] That is, this invention is the measuring method of a thiol group content compound, and offers a method including a production process which detects a change of state of dispersion liquid produced by interaction of a production process; and (2) thiol-group content compound, and a metal particle to which a solution which contains a thiol group content compound in dispersion liquid containing the following production process:(1) metal particle, a solid-state, or a gaseous sample is contacted. According to the desirable mode of this invention, a method of detecting change of a color and/or condensation of a metal particle as a change of state of dispersion liquid is offered.

[0006] A metal particle An above-mentioned way a metal particle is a colloidal state as a still more desirable mode of this invention; The 8th group of an element periodic table, A metal particle An above-mentioned method of containing a metal chosen from a group which consists of the 9th group, the 10th group, the 11th group, and the 12th group as a principal component; The 4th period of an element periodic table, mean particle diameter of the above-mentioned method; metal particle which contains a metal chosen from a group which consists of the 5th period and the 6th period as a principal component -- 0.001 mum -0.5 mum it is -- above-mentioned method; -- a metal particle -- gold -- A thiol group content compound An above-mentioned way the above-mentioned method; metal particle containing silver, copper, and a metal chosen from platinum contains silver as a principal component; Alkyl thiols, An above-mentioned method chosen from aryl thiols, amino acid, its derivatives (a cysteine, glutathione, etc.), and protein is offered.

[0007] Moreover, from another viewpoint of this invention, it is the reagent for measurement of a thiol group content compound, and a reagent containing dispersion liquid containing a metal particle is offered. This reagent is used in order to measure a thiol group content compound by detecting a change of state of dispersion liquid produced by interaction of a thiol group content compound and a metal particle.

According to the desirable mode of this invention, the above-mentioned reagent whose changes of state are change of a color and/or condensation of a metal particle is offered. From still more nearly another viewpoint, dispersion liquid for using it for the above-mentioned all directions method are offered by this invention.

[0008]

[Embodiment of the Invention] The measuring method of the thiol group content compound of this invention includes the production process (the second production process) which detects the change of state which appears in dispersion liquid by the interaction of the production process (the first production process) at which the solution which contains a thiol group content compound to the dispersion liquid containing a metal particle, a solid-state, or a gaseous sample is contacted, and the thiol group content compound and metal particle which are contained in a sample. By the method of this invention, a thiol group content compound can be measured very simple and correctly by detecting the change of state of dispersion liquid. It should be most interpreted as the term "measurement" used in this specification including all the things including quality and a quantum that can offer the information about existence of a thiol group content compound by the wide sense.

[0009] As long as especially the class of thiol group content compound used as the measuring object of the method of this invention is a compound which is not limited but has one piece or two thiol groups or more, what kind of thing is sufficient as it. As a thiol

group content compound, for example Alkyl thiols (Methyl mercaptan, ethyl mercaptan, etc. and aryl) thiols [for example,] For example, (a thiophenol, a thio naphthol, benzyl mercaptan), etc., Amino acid or its derivative (for example, a cysteine, a glutathione, etc.), a peptide compound (for example, the dipeptide compound containing cysteine residue --) Although a tripeptide compound, a tetrapeptide compound, the oligopeptide compound containing five or more amino acid residue, etc. can mention protein (for example, globular protein with which metallothionein and cysteine residue have been arranged on the surface) etc., it is not limited to these.

[0010] If it measures according to the method of this invention, when the thiol group content compound is contained in the sample, between this compound and the metal particle in dispersion liquid, an interaction arises and a change of state detectable in dispersion liquid is caused. The term the "interaction" used in this specification includes the various physicochemical and/or chemical interactions produced between a thiol group content compound and a metal particle, for example, needs to interpret them in a wide sense most including formation of a chemical bond, formation of a complex, adsorption, condensation, oxidation, or reduction. Moreover, the interaction between the material produced according to an enzyme operation, for example, the thiol group content peptide produced according to an operation of a protease, and a metal particle is also included in the above-mentioned interaction.

[0011] What kind of thing may be used for change of the color which happens into dispersion liquid, for example, it can mention coloring, decolorization, concentration change, or color tone change. As for change of a color, it is desirable that it is a change detectable [with means, such as viewing or spectrometry,]. Usually, although change of the color under a visible ray can be observed, the extinction spectrum in an ultraviolet-visible region, an infrared-visible region, or an infrared-visible-ultraviolet region may be measured. Although condensation of a metal particle is generally detectable with means, such as viewing or spectrometry, it is desirable to observe change of the turbidity by condensation etc. by the extinction analysis of a spectrum. It is possible to use a proper analysis of a spectrum according to the class of particle-size metallurgy group of the metal particle to be used etc.

[0012] Especially the metal particle used by the method of this invention is not limited, but may use what kind of thing. For example, it is desirable that a metal particle contains the metal chosen from the group which consists of the 4th period of an element periodic table, the 5th period, and the 6th period as a principal component, and it is desirable that the metal chosen from the group which consists of the 8th group, the 9th group, the 10th group, the 11th group, and the 12th group is included as a principal component. It is the metal of the 4th period, the 5th period, or the 6th period among these metals, and the metal of the 10th group, the 11th group, or the 12th group is still more desirable, and gold, silver, copper, platinum, or palladium is the most desirable. Also in it, gold, silver, and copper are desirable and silver is especially desirable. As silver, colloidal silver is the most desirable. It is also possible to use two or more sorts for manufacture of a metal particle combining the above-mentioned metal, and to use for it as an alloy.

[0013] Although especially an existence condition is not limited, it is desirable that the metal particle exists in the state of stable distribution, for example, it is [that it distributes in a solution and the metal particle should just exist] more desirable that it is a colloidal state. In the case of a colloidal state, it is desirable that for example, the metal particle is

substantially distributed in the state of a globular form particle. Especially for the particle size of a metal particle, although not limited, mean particle diameter is 0.001. μm -0.5 It is desirable that it is the range of μm . The desirable mean particle diameter of a particle is 0.1. μm It is 0.05 micrometers more preferably hereafter. It is 0.03 micrometers especially preferably hereafter. It is the following.

[0014] A hydrophilic macromolecule, a surfactant, antiseptics, a stabilizing agent, etc. may be suitably blended with the dispersion liquid used by the method of this invention as components other than a metal particle. As a hydrophilic macromolecule, it can dissolve in water, and as long as a solution condition is substantially maintainable in a thin condition, what kind of thing may be used. For example, naturally-occurring polymers, such as material of polysaccharide, such as protein, such as gelatin, a collagen, casein, fibronectin, a laminin, and an elastin, and the material; cellulose of the protein origin, starch, agarose, a carrageenan, a dextran, a dexarin, a chitin, chitosan, pectin, and a mannan, and the polysaccharide origin; the gel originating in synthetic macromolecule [, such as poval, polyacrylamide, a polyacrylic acid polyvinyl pyrrolidone a polyethylene glycol, polystyrene sulfonate, and the poly allylamine]; or these etc. can be used. When using gelatin, especially the class of gelatin is not limited, for example, can use cow bone alkali treatment gelatin, pig skin skin alkali treatment gelatin, cow bone acid-treatment gelatin, cow bone FUTARU-ized processing gelatin, pig skin skin acid-treatment gelatin, etc.

[0015] Especially the class of sample used for the method of this invention is not limited. For example, although the aquosity samples for [which was extracted from a waterworks, sewage, waste water, a river etc.] water examinations, soil, sludge, the biological material separated and extracted from the living body, expiration, atmospheric air, soot, exhaust gas, natural gas, a liquefied petroleum gas, etc. can be mentioned, it is not limited to these. As a sample, the biological material separated and extracted from the mammals animal including the liquid containing the thiol group content compound used in fields, such as a chemical research and the chemical industry, a solid-state or a gaseous sample, natural gas, a liquefied petroleum gas, or Homo sapiens can be used suitably, for example.

[0016] As long as thiol group content compounds, such as alkyl thiols or aryl thiols, are included as a sample in the field of a chemical research or the chemical industry, for example among the reagent used for chemosynthesis, reaction mixture, reaction intermediate, a product, or waste fluid, the thing of what kind of gestalt may be used. For example, the air extracted from the inside of a laboratory, a draft chamber, a factory, or various kinds of equipments etc. can be used as a sample. Alkyl thiols are contained or added by natural gas or the liquefied petroleum gas, and it is possible to measure alkyl thiols easily by the method of this invention.

[0017] As a biological material, the organization intercept with which a blood serum, plasma, lymph, crevicular exudate, and destructive venereal disease strange organization or liquid (for example, a rheumatism venereal disease strange synovial fluid, a periodontoclasia organization extract, or crevicular exudate of gum disease), pleural effusion, ascites, cerebrospinal fluid, the abnormality secretion liquid in a mammary gland, the reservoir liquid in the ovary, expectoration, urine, cancer, or cancer is suspected can be mentioned, for example. The sample separated and extracted from the laboratory animal besides extraction samples, such as urine in a medical checkup and

blood, and various kinds of extraction samples in a diagnosis of the illness is contained in a biological material. Laboratory animals are animals other than the Homo sapiens used for an experiment in the field of medicine or pharmaceutical sciences, and a mouse, a rat, a guinea pig, a rabbit, a ferret, a cat, a dog, an ape, a chimpanzee, a goat, a sheep, a cow, a horse, etc. can specifically be mentioned. The cell separated from the mammals animal, the culture of an organization, its culture supernatant, etc. are included by the biological material.

[0018] Thin sectioning or after judging finely, and using as it is or homogenizing, a component may be extracted using water or the buffer solution, or it may compress, and tissue fluid may be made to ooze, when a biological material is an organization. the case where the synovial membrane liquid extracted from the patient of rheumatic arthritis is used as a biological material -- synovial membrane **** 5-100microL -- what is necessary is just to use about [20micro] L preferably In using the crevicular exudate of gum disease as a sample, it inserts a filter paper into a gingival sulcus, and it is abbreviation. 5-10microL The crevicular exudate of a degree can be extracted and the method immersed in the dispersion liquid of this invention in this filter paper can be adopted. Crevicular exudate may be extracted from a filter paper after extraction of crevicular exudate using distilled water or the proper buffer solutions (for example, 50 mM Tris-HCl, pH 7.5, 10 mM CaCl₂, 0.2 MNaCl, etc.) if needed, and an extract may be dropped at the dispersion liquid of this invention.

[0019] Although especially the solvent of the dispersion liquid of this invention is not limited, water, a methanol, ethanol, isopropyl alcohol, ethylene glycol, a glycerol, a polyethylene glycol, dioxane, N-methyl pyrrolidone, dimethyl SUHOKISHIDO, dimethylformamide, dimethylacetamides, or those mixed solvents can be used, for example. Although not limited especially about pH in the case of using water for a solvent, about five to eight pH is desirable. Although the optimal pH which gives the greatest change of state according to the class of thiol group content compound of the measuring object may differ, this contractor can choose proper pH easily. Although the preparation method of the suspension when using a metal particle by the colloidal state does not have especially limitation, it is possible to adopt suitably the distributed method currently used widely, for example in the technical field of a photographic film etc.

[0020] If the case where colloidal silver is used as a metal particle is explained, since the black colloidal silver the yellow colloidal silver as an object for yellow filters and for anti halation is generally usually used, for example in the field of silver halide color photography sensitive material, colloidal silver can use these colloidal silver for this invention. Moreover, in addition to these, you may be colloidal silver of sour orange brown or *****. among these -- the maximum absorption wavelength -- 400nm from -- 500nm Especially the thing for which yellow colloidal silver is used is desirable.

[0021] The method learned from the former as the preparation method of colloidal silver, for example, the method of returning fusibility silver salt by hydroquinone in the gelatin solution indicated by the U.S. Pat. No. 2,688,601 specification, the method of returning the poorly soluble silver salt indicated by the German patent No. 1,096,193 specification by the hydrazine, the method of returning to silver with a tannic acid as indicated by the U.S. Pat. No. 2,921,914 specification, the method of forming a silver granule child by electroless deposition as indicated by JP,5-134358,A, etc. can use. Moreover, Wiley & Sons, New York, the 1933 issue, and Weiser work Colloidal Elements The preparation

method of the yellow colloidal silver by the dextrin reduction of indicated Carey Le may be used.

[0022] In case the dispersion liquid of this invention are manufactured, in addition to the component explained above, components, such as a color, a pigment, antiseptics, a dispersant, and a stabilizing agent, may be blended suitably. Especially if the interaction of a thiol group content compound and a metal particle is not affected substantially, it will not be limited, but such a component can choose and use a proper thing. As a color, the color (the 9th page color concretely shown by the chemical structure type to 63 the 47th page from I-1) indicated by JP,6-102624,A can be used, for example, and the addition method of a color can adopt the method (method concretely explained by the 12th page paragraph number [0044] from the 11th page paragraph number [0037]) indicated by JP,5-313307,A. Although especially the store method of the dispersion liquid of this invention is not limited, it is desirable to save, for example at the temperature of about 5-15 degrees C. There is especially no limitation also about a conservation container, and the container for the hermetic container for inspection reagents, a well-closed container or the emulsion for photographs, and processing agents, a light resistant container, etc. can be used preferably.

[0023] the range of the room temperature although especially the gestalt of operation of the method of this invention is not limited, after contacting the dispersion liquid and the sample of this invention, for example to 80 degrees C -- it is -- desirable -- 37 degrees C for [1 minute] - 24 hours -- desirable -- for [5 minutes] - 3 hours -- further -- desirable - during 5 minutes -- what is necessary is just to incubate for about 1 hour When a thiol group content compound is contained in a sample, an interaction arises between the metal particles of a solution, and change of a color or condensation of a metal particle is caused in a solution. Although change of a color and condensation of a metal particle may be caused in coincidence, either of those change or both are detectable. When using the solution sample containing an enzyme, the reactant by enzyme operation may be detected.

[0024]

[Example] Hereafter, although an example explains this invention still more concretely, the range of this invention is not limited to these examples.

Example 1: manufacture (a) of the dispersion liquid for measurement of a thiol group content compound Aqueous solution 18 g Containing the dextrin which adjusted the creation pH of a colloidal silver emulsion to 11.0 700 mL Silver nitrate 17 g the included aqueous solution -- adding -- gelatin -- adding -- flow KYURESHON well-known at 30 degrees C -- it rinsed by law and created by adding gelatin further and heating at 60 degrees C. The obtained colloidal silver emulsion was yellow in the state of the solution. The emulsion carried out refrigeration conservation.

(b) Creation colloidal silver emulsion of dispersion liquid 1 g was diluted and distributed at 40 degrees C at pure water 100 mL, and dispersion liquid were obtained. The silver concentration of this solution was 1.9 mmol/L. In addition, the surfactant was used if needed.

[0025] Example 2: as a sample containing the measurement thiol group content compound of the thiol group content compound using colloidal silver dispersion liquid, the solution which contains ethyl mercaptan, phenyl mercaptan, a cysteine, a glutathione, and metallothionein by the concentration of 0.1 mmol/L to 25 mmol/L, respectively was

used. As a biological material, the supernatant liquid which cultivated the frozen section of a breast cancer organization and U937 cell was used. Liquid sample 0.1 mL was dropped at dispersion-liquid 0.9 mL obtained in Example 1. The organization sample homogenized the suitable amount with little water, and mixed supernatant liquid with colloidal silver dispersion liquid. It puts into the tube which can seal the mixed liquor of each sample and colloidal silver dispersion liquid, and is [37-degree C] under water bath. After incubating for 10 to 60 minutes, the judgment by viewing or the judgment by measurement of the spectral extinction by the spectrophotometer was performed to each sample, and change of a color and condensation of a particle were evaluated.

[0026] Consequently, the red tinctorial change appeared visually also about which sample. Coloring strong against a short time was shown, so that concentration was high about each thiols solution. Moreover, when the spectrophotometer estimated the absorbance in 510 nm, absorption became strong, so that incubation time amount was long, and absorption became strong at the concentration dependence target. About the breast cancer organization, the sample like a cancerous region hardly colored in a surrounding normal portion to strong coloring having been shown.

[0027]

[Effect of the Invention] The method of this invention can measure a liquid, a solid-state, or the CHIO radical content compound in a gaseous sample correctly and simple, and has the feature that it can judge in a short time compared with the conventional method.

OPERATION

The term an "interaction" includes the various physicochemical and/or chemical interactions produced between a thiol group content compound and a metal particle, for example, needs to interpret them in a wide sense most including formation of a chemical bond, formation of a complex, adsorption, condensation, oxidation, or reduction. Moreover, the interaction between the material produced according to an enzyme operation, for example, the thiol group content peptide produced according to an operation of a protease, and a metal particle is also included in the above-mentioned interaction.

[0011] What kind of thing may be used for change of the color which happens into dispersion liquid, for example, it can mention coloring, decolorization, concentration change, or color tone change. As for change of a color, it is desirable that it is a change detectable [with means, such as viewing or spectrometry,]. Usually, although change of the color under a visible ray can be observed, the extinction spectrum in an ultraviolet-visible region, an infrared-visible region, or an infrared-visible-ultraviolet region may be measured. Although condensation of a metal particle is generally detectable with means, such as viewing or spectrometry, it is desirable to observe change of the turbidity by condensation etc. by the extinction analysis of a spectrum. It is possible to use a proper analysis of a spectrum according to the class of particle-size metallurgy group of the metal particle to be used etc.

[0012] Especially the metal particle used by the method of this invention is not limited, but may use what kind of thing. For example, it is desirable that a metal particle contains the metal chosen from the group which consists of the 4th period of an element periodic table, the 5th period, and the 6th period as a principal component, and it is desirable that the metal chosen from the group which consists of the 8th group, the 9th group, the 10th

group, the 11th group, and the 12th group is included as a principal component. It is the metal of the 4th period, the 5th period, or the 6th period among these metals, and the metal of the 10th group, the 11th group, or the 12th group is still more desirable, and gold, silver, copper, platinum, or palladium is the most desirable. Also in it, gold, silver, and copper are desirable and silver is especially desirable. As silver, colloidal silver is the most desirable. It is also possible to use two or more sorts for manufacture of a metal particle combining the above-mentioned metal, and to use for it as an alloy.

[0013] Although especially an existence condition is not limited, it is desirable that the metal particle exists in the state of stable distribution, for example, it is [that it distributes in a solution and the metal particle should just exist] more desirable that it is a colloidal state. In the case of a colloidal state, it is desirable that for example, the metal particle is substantially distributed in the state of a globular form particle. Especially for the particle size of a metal particle, although not limited, mean particle diameter is 0.001. μm -0.5 It is desirable that it is the range of μm . The desirable mean particle diameter of a particle is 0.1. μm It is 0.05 micrometers more preferably hereafter. It is 0.03 micrometers especially preferably hereafter. It is the following.

[0014] A hydrophilic macromolecule, a surfactant, antiseptics, a stabilizing agent, etc. may be suitably blended with the dispersion liquid used by the method of this invention as components other than a metal particle. As a hydrophilic macromolecule, it can dissolve in water, and as long as a solution condition is substantially maintainable in a thin condition, what kind of thing may be used. For example, naturally-occurring polymers, such as material of polysaccharide, such as protein, such as gelatin, a collagen, casein, fibronectin, a laminin, and an elastin, and the material; cellulose of the protein origin, starch, agarose, a carrageenan, a dextran, a dextrin, a chitin, chitosan, pectin, and a mannan, and the polysaccharide origin; the gel originating in synthetic macromolecule [, such as poval, polyacrylamide, a polyacrylic acid polyvinyl pyrrolidone a polyethylene glycol, polystyrene sulfonate, and the poly allylamine]; or these etc. can be used. When using gelatin, especially the class of gelatin is not limited, for example, can use cow bone alkali treatment gelatin, pig skin skin alkali treatment gelatin, cow bone acid-treatment gelatin, cow bone FUTARU-ized processing gelatin, pig skin skin acid-treatment gelatin, etc.

[0015] Especially the class of sample used for the method of this invention is not limited. For example, although the aquosity samples for [which was extracted from a waterworks, sewage, waste water, a river etc.] water examinations, soil, sludge, the biological material separated and extracted from the living body, expiration, atmospheric air, soot, exhaust gas, natural gas, a liquefied petroleum gas, etc. can be mentioned, it is not limited to these. As a sample, the biological material separated and extracted from the mammals animal including the liquid containing the thiol group content compound used in fields, such as a chemical research and the chemical industry, a solid-state or a gaseous sample, natural gas, a liquefied petroleum gas, or Homo sapiens can be used suitably, for example.

[0016] As long as thiol group content compounds, such as alkyl thiols or aryl thiols, are included as a sample in the field of a chemical research or the chemical industry, for example among the reagent used for chemosynthesis, reaction mixture, reaction intermediate, a product, or waste fluid, the thing of what kind of gestalt may be used. For example, the air extracted from the inside of a laboratory, a draft chamber, a factory, or

various kinds of equipments etc. can be used as a sample. Alkyl thiols are contained or added by natural gas or the liquefied petroleum gas, and it is possible to measure alkyl thiols easily by the method of this invention.

[0017] As a biological material, the organization intercept with which a blood serum, plasma, lymph, crevicular exudate, and destructive venereal disease strange organization or liquid (for example, a rheumatism venereal disease strange synovial fluid, a periodontoclasia organization extract, or crevicular exudate of gum disease), pleural effusion, ascites, cerebrospinal fluid, the abnormality secretion liquid in a mammary gland, the reservoir liquid in the ovary, expectoration, urine, cancer, or cancer is suspected can be mentioned, for example. The sample separated and extracted from the laboratory animal besides extraction samples, such as urine in a medical checkup and blood, and various kinds of extraction samples in a diagnosis of the illness is contained in a biological material. Laboratory animals are animals other than the Homo sapiens used for an experiment in the field of medicine or pharmaceutical sciences, and a mouse, a rat, a guinea pig, a rabbit, a ferret, a cat, a dog, an ape, a chimpanzee, a goat, a sheep, a cow, a horse, etc. can specifically be mentioned. The cell separated from the mammals animal, the culture of an organization, its culture supernatant, etc. are included by the biological material.

[0018] Thin sectioning or after judging finely, and using as it is or homogenizing, a component may be extracted using water or the buffer solution, or it may compress, and tissue fluid may be made to ooze, when a biological material is an organization. the case where the synovial membrane liquid extracted from the patient of rheumatic arthritis is used as a biological material -- synovial membrane **** 5-100microL -- what is necessary is just to use about [20micro] L preferably In using the crevicular exudate of gum disease as a sample, it inserts a filter paper into a gingival sulcus, and it is abbreviation. 5-10microL The crevicular exudate of a degree can be extracted and the method immersed in the dispersion liquid of this invention in this filter paper can be adopted. Crevicular exudate may be extracted from a filter paper after extraction of crevicular exudate using distilled water or the proper buffer solutions (for example, 50 mM Tris-HCl, pH 7.5, 10 mM CaCl₂, 0.2 MNaCl, etc.) if needed, and an extract may be dropped at the dispersion liquid of this invention.

[0019] Although especially the solvent of the dispersion liquid of this invention is not limited, water, a methanol, ethanol, isopropyl alcohol, ethylene glycol, a glycerol, a polyethylene glycol, dioxane, N-methyl pyrrolidone, dimethyl SUHOKISHIDO, dimethylformamide, dimethylacetamides, or those mixed solvents can be used, for example. Although not limited especially about pH in the case of using water for a solvent, about five to eight pH is desirable. Although the optimal pH which gives the greatest change of state according to the class of thiol group content compound of the measuring object may differ, this contractor can choose proper pH easily. Although the preparation method of the suspension when using a metal particle by the colloidal state does not have especially limitation, it is possible to adopt suitably the distributed method currently used widely, for example in the technical field of a photographic film etc.

[0020] If the case where colloidal silver is used as a metal particle is explained, since the black colloidal silver the yellow colloidal silver as an object for yellow filters and for anti halation is generally usually used, for example in the field of silver halide color photography sensitive material, colloidal silver can use these colloidal silver for this

invention. Moreover, in addition to these, you may be colloidal silver of sour orange brown or *****. among these -- the maximum absorption wavelength -- 400nm from -- 500nm Especially the thing for which yellow colloidal silver is used is desirable.

[0021] The method learned from the former as the preparation method of colloidal silver, for example, the method of returning fusibility silver salt by hydroquinone in the gelatin solution indicated by the U.S. Pat. No. 2,688,601 specification, the method of returning the poorly soluble silver salt indicated by the German patent No. 1,096,193 specification by the hydrazine, the method of returning to silver with a tannic acid as indicated by the U.S. Pat. No. 2,921,914 specification, the method of forming a silver granule child by electroless deposition as indicated by JP,5-134358,A, etc. can use. Moreover, Wiley & Sons, New York, the 1933 issue, and Weiser work Colloidal Elements The preparation method of the yellow colloidal silver by the dextrin reduction of indicated Carey Le may be used.

[0022] In case the dispersion liquid of this invention are manufactured, in addition to the component explained above, components, such as a color, a pigment, antiseptics, a dispersant, and a stabilizing agent, may be blended suitably. Especially if the interaction of a thiol group content compound and a metal particle is not affected substantially, it will not be limited, but such a component can choose and use a proper thing. As a color, the color (the 9th page color concretely shown by the chemical structure type to 63 the 47th page from I-1) indicated by JP,6-102624,A can be used, for example, and the addition method of a color can adopt the method (method concretely explained by the 12th page paragraph number [0044] from the 11th page paragraph number [0037]) indicated by JP,5-313307,A. Although especially the store method of the dispersion liquid of this invention is not limited, it is desirable to save, for example at the temperature of about 5-15 degrees C. There is especially no limitation also about a conservation container, and the container for the hermetic container for inspection reagents, a well-closed container or the emulsion for photographs, and processing agents, a light resistant container, etc. can be used preferably.

[0023] the range of the room temperature although especially the gestalt of operation of the method of this invention is not limited, after contacting the dispersion liquid and the sample of this invention, for example to 80 degrees C -- it is -- desirable -- 37 degrees C for [1 minute] - 24 hours -- desirable -- for [5 minutes] - 3 hours -- further -- desirable - during 5 minutes -- what is necessary is just to incubate for about 1 hour When a thiol group content compound is contained in a sample, an interaction arises between the metal particles of a solution, and change of a color or condensation of a metal particle is caused in a solution. Although change of a color and condensation of a metal particle may be caused in coincidence, either of those change or both are detectable. When using the solution sample containing an enzyme, the reactant by enzyme operation may be detected.

EXAMPLE

[Example] Hereafter, although an example explains this invention still more concretely, the range of this invention is not limited to these examples.

Example 1: manufacture (a) of the dispersion liquid for measurement of a thiol group content compound Aqueous solution 18 g Containing the dextrin which adjusted the

creation pH of a colloidal silver emulsion to 11.0 700 mL Silver nitrate 17 g the included aqueous solution -- adding -- gelatin -- adding -- flow KYURESHON well-known at 30 degrees C -- it rinsed by law and created by adding gelatin further and heating at 60 degrees C. The obtained colloidal silver emulsion was yellow in the state of the solution. The emulsion carried out refrigeration conservation.

(b) Creation colloidal silver emulsion of dispersion liquid 1 g was diluted and distributed at 40 degrees C at pure water 100 mL, and dispersion liquid were obtained. The silver concentration of this solution was 1.9 mmol/L. In addition, the surfactant was used if needed.

[0025] Example 2: as a sample containing the measurement thiol group content compound of the thiol group content compound using colloidal silver dispersion liquid, the solution which contains ethyl mercaptan, phenyl mercaptan, a cysteine, a glutathione, and metallothionein by the concentration of 0.1 mmol/L to 25 mmol/L, respectively was used. As a biological material, the supernatant liquid which cultivated the frozen section of a breast cancer organization and U937 cell was used. Liquid sample 0.1 mL was dropped at dispersion-liquid 0.9 mL obtained in Example 1. The organization sample homogenized the suitable amount with little water, and mixed supernatant liquid with colloidal silver dispersion liquid. It puts into the tube which can seal the mixed liquor of each sample and colloidal silver dispersion liquid, and is [37-degree C] under water bath. After incubating for 10 to 60 minutes, the judgment by viewing or the judgment by measurement of the spectral extinction by the spectrophotometer was performed to each sample, and change of a color and condensation of a particle were evaluated.

[0026] Consequently, the red tinctorial change appeared visually also about which sample. Coloring strong against a short time was shown, so that concentration was high about each thiols solution. Moreover, when the spectrophotometer estimated the absorbance in 510 nm, absorption became strong, so that incubation time amount was long, and absorption became strong at the concentration dependence target. About the breast cancer organization, the sample like a cancerous region hardly colored in a surrounding normal portion to strong coloring having been shown.